

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-67. (Canceled)

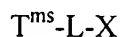
68. (Currently Amended) A method comprising:

(a) providing nucleic acid fragments, each fragment having cleavably attached thereto a mass tag;

(b) separating the tagged fragments on the basis of fragment charge, sequential length, size or shape;

(c) placing a charge on the tag and cleaving the tag from the fragment, where the charge is placed on the tag prior to, during, or after cleaving the tag from the fragment; and

(d) characterizing each tag by mass spectrometry. ~~The method according to claim 59~~ wherein at least one tagged nucleic acid fragment is a compound of the formula:



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a unique T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid; and

X is a nucleic acid fragment attached to L at other than the 3' end of the nucleic acid fragment;

with the provisos that the compound is not bonded to a solid support nor has a mass of less than 250 daltons.

69. (Previously Presented) The method according to claim 68 wherein T^{ms} has a mass of from 15 to 10,000 daltons and a molecular formula of $C_{1-500}N_{0-100}O_{0-100}S_{0-10}P_{0-10}H_{\alpha}F_{\beta}I_{\delta}$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, P and S atoms.

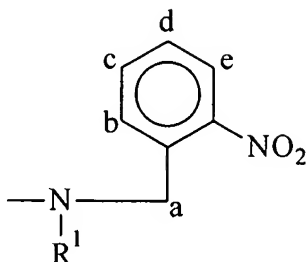
70. (Previously Presented) The method according to claim 68 wherein T^{ms} and L are bonded together through a functional group selected from amide, ester, ether, amine, sulfide, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate, Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate, phosphoramidate, phosphonamide, sulfonate, sulfonamide or carbon-carbon bond.

71. (Previously Presented) The method according to claim 70 wherein the functional group is selected from amide, ester, amine, urea and carbamate.

72. (Previously Presented) The method according to claim 68 wherein L is selected from L^{hv} , L^{acid} , L^{base} , $L^{[O]}$, $L^{[R]}$, L^{enz} , L^{elc} , L^{Δ} and L^{ss} , where actinic radiation, acid, base, oxidation, reduction, enzyme, electrochemical, thermal and thiol exchange, respectively, cause the T^{ms} -containing moiety to be cleaved from the remainder of the molecule.

73. (Previously Presented) The method according to claim 72 wherein L^{hv} has the formula $L^1-L^2-L^3$, wherein L^2 is a molecular fragment that absorbs actinic radiation to promote the cleavage of T^{ms} from X, and L^1 and L^3 are independently a direct bond or an organic moiety, where L^1 separates L^2 from T^{ms} and L^3 separates L^2 from X, and neither L^1 nor L^3 undergo bond cleavage when L^2 absorbs the actinic radiation.

74. (Previously Presented) The method according to claim 73 wherein -
 L^2 has the formula:

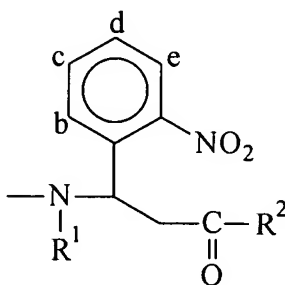


with one carbon atom at positions a, b, c, d or e being substituted with -L³-X and optionally one or more of positions b, c, d or e being substituted with alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R¹ is hydrogen or hydrocarbyl.

75. (Previously Presented) The method according to claim 74 wherein
 X is $\text{—}\overset{\text{O}}{\underset{\parallel}{\text{C}}}\text{—R}^2$ and R² is a nucleic acid fragment.

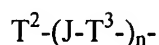
76. (Previously Presented) The method according to claim 73 wherein
 L³ is selected from a direct bond, a hydrocarbylene, -O-hydrocarbylene, and hydrocarbylene-(O-hydrocarbylene)_n-, and n is an integer ranging from 1 to 10.

77. (Previously Presented) The method according to claim 68 wherein -
 L-X has the formula:



wherein one or more of positions b, c, d or e is substituted with hydrogen, alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R¹ is hydrogen or hydrocarbyl, and R² is a nucleic acid fragment.

78. (Previously Presented) The method according to claim 68 wherein T^{ms} has the formula:



T² is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 15 to 500 daltons;

T³ is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 50 to 1000 daltons;

J is a direct bond or a functional group selected from amide, ester, amine, sulfide, ether, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate, Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate, phosphoramidate, phosphonamide, sulfonate, sulfonamide or carbon-carbon bond; and

n is an integer ranging from 1 to 50, and when n is greater than 1, each T³ and J is independently selected.

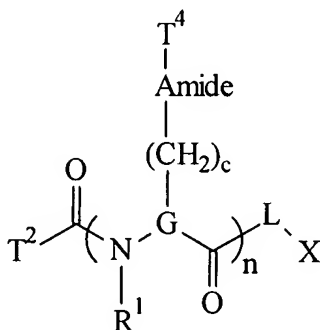
79. (Previously Presented) The method according to claim 78 wherein T² is selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, hydrocarbyl-NH-hydrocarbylene, hydrocarbyl-amide-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene, hydrocarbylacetylhydrocarbylene, heterocyclylhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus, substituted heterocyclylhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus and the substituents are selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-NH-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene and

hydrocarbylacyl-hydrocarbylene, as well as derivatives of any of the foregoing wherein one or more hydrogens is replaced with an equal number of fluorides.

80. (Previously Presented) The method according to claim 78 wherein T^3 has the formula $-G(R^2)-$, G is C_{1-6} alkylene having a single R^2 substituent, and R^2 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aryl-substituted alkenyl or alkynyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, biaryl, alkoxy, alkenoxy, alkynoxy, aralkoxy, aryl-substituted alkenoxy or alkynoxy, alkylamino, alkenylamino or alkynylamino, aryl-substituted alkylamino, aryl-substituted alkenylamino or alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, N-arylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, aminocarbonyl-substituted alkyl, heterocyclyl, heterocyclyl-substituted alkyl, heterocyclyl-substituted amino, carboxyalkyl substituted aralkyl, oxocarbocyclyl-fused aryl and heterocyclylalkyl; cycloalkenyl, aryl-substituted alkyl and, aralkyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, aralkoxy-substituted alkyl, alkoxy-substituted alkyl, aralkoxy-substituted alkyl, amino-substituted alkyl, (aryl-substituted alkyloxycarbonylamino)-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, hydrocarbylacylamino-substituted alkyl, heterocyclylacylamino-substituted alkyl, hydrocarbyl-substituted-heterocyclylacylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, arylsulfonylamino-substituted alkyl, morpholino-alkyl, thiomorpholino-alkyl, morpholino carbonyl-substituted alkyl, thiomorpholinocarbonyl-substituted alkyl, [N-(alkyl, alkenyl or alkynyl)- or N,N-[dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino]carbonyl-substituted alkyl, heterocyclylaminocarbonyl, heterocyclylalkyleneaminocarbonyl, heterocyclylaminocarbonyl-substituted alkyl, heterocyclylalkyleneaminocarbonyl-substituted alkyl, N,N-[dialkyl]alkyleneaminocarbonyl, N,N-[dialkyl]alkyleneaminocarbonyl-substituted alkyl, alkyl-substituted heterocyclylcarbonyl, alkyl-substituted heterocyclylcarbonyl-alkyl, carboxyl-substituted alkyl, dialkylamino-substituted acylaminoalkyl and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-

leucine, norleucine, phenylalanine, tyrosine, tryptophan, proline, alanine, ornithine, histidine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine; alynyl, heterocyclylcarbonyl, aminocarbonyl, amido, mono- or dialkylaminocarbonyl, mono- or diarylaminocarbonyl, alkylarylaminocarbonyl, diarylaminocarbonyl, mono- or diacylaminocarbonyl, aromatic or aliphatic acyl, alkyl optionally substituted by substituents selected from amino, carboxy, hydroxy, mercapto, mono- or dialkylamino, mono- or diarylamino, alkylarylamino, diarylamino, mono- or diacylamino, alkoxy, alkenoxy, aryloxy, thioalkoxy, thioalkenoxo, thioalkynoxo, thioaryloxy and heterocyclyl.

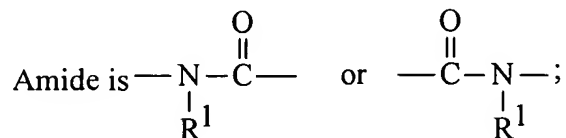
81. (Currently Amended) The method according to claim 78 having the formula:



wherein

G is $(CH_2)_{1-6}$ wherein a hydrogen on one and only one of the CH_2 groups of each G is replaced with $-(CH_2)_c\text{-Amide-}T^4$;

T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_\alpha F_\beta I_\delta$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms;



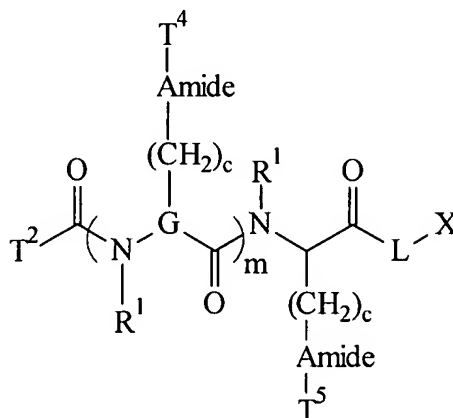
R^1 is hydrogen or C_{1-10} alkyl;

c is an integer ranging from 0 to 4;

~~X is defined according to claim 1; and~~

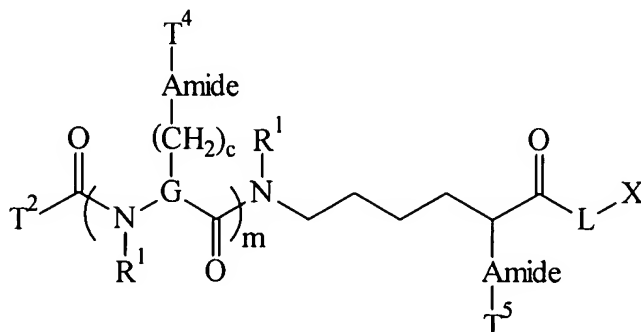
n is an integer ranging from 1 to 50 such that when n is greater than 1, G, c, Amide, R¹ and T⁴ are independently selected.

82. (Previously Presented) The method according to claim 81 having the formula:



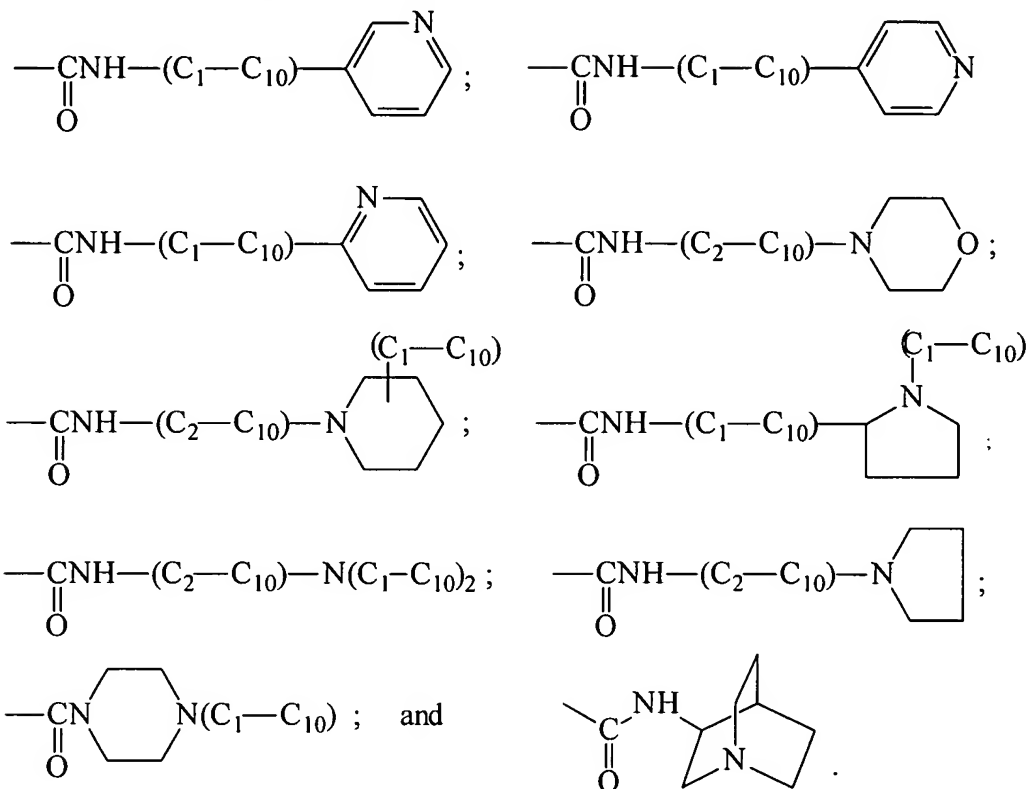
wherein T⁵ is an organic moiety of the formula C₁₋₂₅N₀₋₉O₀₋₉S₀₋₃P₀₋₃H_αF_βI_δ wherein the sum of α, β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms; and T⁵ includes a tertiary or quaternary amine or an organic acid; and m is an integer ranging from 0-49.

83. (Currently Amended) The method according to claim 68 having the formula:





85. (Previously Presented) The method according to any of claims 82 and 83 wherein -Amide-T⁵ is selected from:



86. (Previously Presented) The method according to any one of claims 78-82 wherein T² has the structure which results when one of the following organic acids is condensed with an amine group to form T²-C(=O)-N(R¹)-: Formic acid, Acetic acid, Propionic acid, Propionic acid, Fluoroacetic acid, 2-Butynoic acid, Cyclopropanecarboxylic acid, Butyric acid, Methoxyacetic acid, Difluoroacetic acid, 4-Pentynoic acid, Cyclobutanecarboxylic acid, 3,3-Dimethylacrylic acid, Valeric acid, N,N-Dimethylglycine, N-Formyl-Gly-OH, Ethoxyacetic acid, (Methylthio)acetic acid, Pyrrole-2-carboxylic acid, 3-Furoic acid, Isoxazole-5-carboxylic acid, trans-3-Hexenoic acid, Trifluoroacetic acid, Hexanoic acid, Ac-Gly-OH, 2-Hydroxy-2-methylbutyric acid, Benzoic acid, Nicotinic acid, 2-Pyrazinecarboxylic acid, 1-Methyl-2-pyrrolicarboxylic acid, 2-Cyclopentene-1-acetic acid, Cyclopentylacetic acid, (S)-(-)-2-Pyrrolidone-5-carboxylic acid, N-Methyl-L-proline, Heptanoic acid, Ac-b-Ala-OH, 2-Ethyl-2-

hydroxybutyric acid, 2-(2-Methoxyethoxy)acetic acid, p-Toluic acid, 6-Methylnicotinic acid, 5-Methyl-2-pyrazinecarboxylic acid, 2,5-Dimethylpyrrole-3-carboxylic acid, 4-Fluorobenzoic acid, 3,5-Dimethylisoxazole-4-carboxylic acid, 3-Cyclopentylpropionic acid, Octanoic acid, N,N-Dimethylsuccinamic acid, Phenylpropionic acid, Cinnamic acid, 4-Ethylbenzoic acid, p-Anisic acid, 1,2,5-Trimethylpyrrole-3-carboxylic acid, 3-Fluoro-4-methylbenzoic acid, Ac-DL-Propargylglycine, 3-(Trifluoromethyl)butyric acid, 1-Piperidinepropionic acid, N-Acetylproline, 3,5-Difluorobenzoic acid, Ac-L-Val-OH, Indole-2-carboxylic acid, 2-Benzofurancarboxylic acid, Benzotriazole-5-carboxylic acid, 4-n-Propylbenzoic acid, 3-Dimethylaminobenzoic acid, 4-Ethoxybenzoic acid, 4-(Methylthio)benzoic acid, N-(2-Furoyl)glycine, 2-(Methylthio)nicotinic acid, 3-Fluoro-4-methoxybenzoic acid, Tfa-Gly-OH, 2-Napthoic acid, Quinaldic acid, Ac-L-Ile-OH, 3-Methylindene-2-carboxylic acid, 2-Quinoxalinecarboxylic acid, 1-Methylindole-2-carboxylic acid, 2,3,6-Trifluorobenzoic acid, N-Formyl-L-Met-OH, 2-[2-(2-Methoxyethoxy)ethoxy]acetic acid, 4-n-Butylbenzoic acid, N-Benzoylglycine, 5-Fluoroindole-2-carboxylic acid, 4-n-Propoxybenzoic acid, 4-Acetyl-3,5-dimethyl-2-pyrrolecarboxylic acid, 3,5-Dimethoxybenzoic acid, 2,6-Dimethoxynicotinic acid, Cyclohexanepentanoic acid, 2-Naphthylacetic acid, 4-(1H-Pyrrol-1-yl)benzoic acid, Indole-3-propionic acid, m-Trifluoromethylbenzoic acid, 5-Methoxyindole-2-carboxylic acid, 4-Pentylbenzoic acid, Bz-b-Ala-OH, 4-Diethylaminobenzoic acid, 4-n-Butoxybenzoic acid, 3-Methyl-5-CF₃-isoxazole-4-carboxylic acid, (3,4-Dimethoxyphenyl)acetic acid, 4-Biphenylcarboxylic acid, Pivaloyl-Pro-OH, Octanoyl-Gly-OH, (2-Naphthoxy)acetic acid, Indole-3-butyric acid, 4-(Trifluoromethyl)phenylacetic acid, 5-Methoxyindole-3-acetic acid, 4-(Trifluoromethoxy)benzoic acid, Ac-L-Phe-OH, 4-Pentyloxybenzoic acid, Z-Gly-OH, 4-Carboxy-N-(fur-2-ylmethyl)pyrrolidin-2-one, 3,4-Diethoxybenzoic acid, 2,4-Dimethyl-5-CO₂Et-pyrrole-3-carboxylic acid, N-(2-Fluorophenyl)succinamic acid, 3,4,5-Trimethoxybenzoic acid, N-Phenylanthranilic acid, 3-Phenoxybenzoic acid, Nonanoyl-Gly-OH, 2-Phenoxypyridine-3-carboxylic acid, 2,5-Dimethyl-1-phenylpyrrole-3-carboxylic acid, trans-4-(Trifluoromethyl)cinnamic acid, (5-Methyl-2-phenyloxazol-4-yl)acetic acid, 4-(2-Cyclohexenyloxy)benzoic acid, 5-Methoxy-2-methylindole-3-acetic acid, trans-4-Cotininecarboxylic acid, Bz-5-Aminovaleric acid, 4-Hexyloxybenzoic acid, N-(3-

Methoxyphenyl)succinamic acid, Z-Sar-OH, 4-(3,4-Dimethoxyphenyl)butyric acid, Ac-o-Fluoro-DL-Phe-OH, N-(4-Fluorophenyl)glutaramic acid, 4'-Ethyl-4-biphenylcarboxylic acid, 1,2,3,4-Tetrahydroacridinecarboxylic acid, 3-Phenoxyphenylacetic acid, N-(2,4-Difluorophenyl)succinamic acid, N-Decanoyl-Gly-OH, (+)-6-Methoxy-a-methyl-2-naphthaleneacetic acid, 3-(Trifluoromethoxy)cinnamic acid, N-Formyl-DL-Trp-OH, (R)-(+)-a-Methoxy-a-(trifluoromethyl)phenylacetic acid, Bz-DL-Leu-OH, 4-(Trifluoromethoxy)phenoxyacetic acid, 4-Heptyloxybenzoic acid, 2,3,4-Trimethoxycinnamic acid, 2,6-Dimethoxybenzoyl-Gly-OH, 3-(3,4,5-Trimethoxyphenyl)propionic acid, 2,3,4,5,6-Pentafluorophenoxyacetic acid, N-(2,4-Difluorophenyl)glutaramic acid, N-Undecanoyl-Gly-OH, 2-(4-Fluorobenzoyl)benzoic acid, 5-Trifluoromethoxyindole-2-carboxylic acid, N-(2,4-Difluorophenyl)diglycolamic acid, Ac-L-Trp-OH, Tfa-L-Phenylglycine-OH, 3-Iodobenzoic acid, 3-(4-n-Pentylbenzoyl)propionic acid, 2-Phenyl-4-quinolinecarboxylic acid, 4-Octyloxybenzoic acid, Bz-L-Met-OH, 3,4,5-Triethoxybenzoic acid, N-Lauroyl-Gly-OH, 3,5-Bis(trifluoromethyl)benzoic acid, Ac-5-Methyl-DL-Trp-OH, 2-Iodophenylacetic acid, 3-Iodo-4-methylbenzoic acid, 3-(4-n-Hexylbenzoyl)propionic acid, N-Hexanoyl-L-Phe-OH, 4-Nonyloxybenzoic acid, 4'-(Trifluoromethyl)-2-biphenylcarboxylic acid, Bz-L-Phe-OH, N-Tridecanoyl-Gly-OH, 3,5-Bis(trifluoromethyl)phenylacetic acid, 3-(4-n-Heptylbenzoyl)propionic acid, N-Hepytanoyl-L-Phe-OH, 4-Decyloxybenzoic acid, N-(α,α,α -trifluoro-m-tolyl)anthranilic acid, Niflumic acid, 4-(2-Hydroxyhexafluoroisopropyl)benzoic acid, N-Myristoyl-Gly-OH, 3-(4-n-Octylbenzoyl)propionic acid, N-Octanoyl-L-Phe-OH, 4-Undecyloxybenzoic acid, 3-(3,4,5-Trimethoxyphenyl)propionyl-Gly-OH, 8-Iodonaphthoic acid, N-Pentadecanoyl-Gly-OH, 4-Dodecyloxybenzoic acid, N-Palmitoyl-Gly-OH, and N-Stearoyl-Gly-OH.

87. (New) The method according to claim 68 wherein the detection of the tags is by mass spectrometry, infrared spectrometry, ultraviolet spectrometry or potentiostatic amperometry.

88. (New) The method according to claim 68 wherein the tagged fragments are separated in step (b) by a method selected from gel electrophoresis, capillary electrophoresis, micro-channel electrophoresis and HPLC.

89. (New) The method according to claim 68 wherein the tagged fragments are cleaved in step (c) by a method selected from oxidation, reduction, acid-labile, base-labile, enzymatic, electrochemical, thermal, thiol exchange and photolabile methods.

90. (New) The method according to claim 68 wherein the tags are detected by time-of-flight mass spectrometry, quadrupole mass spectrometry, magnetic sector mass spectrometry or electric sector mass spectrometry.

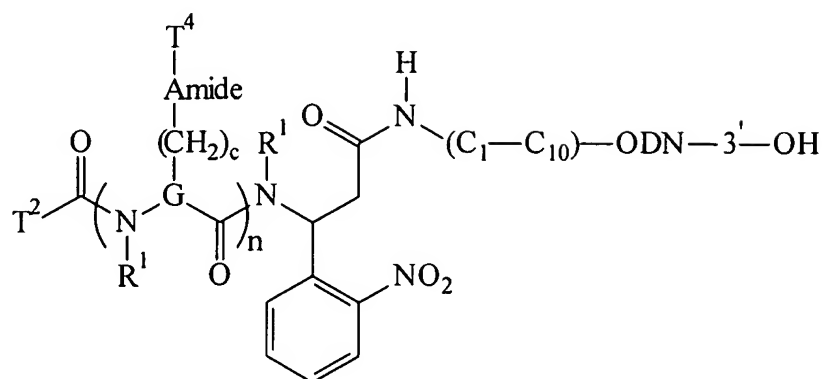
91. (New) The method according to claim 68 wherein step (a) provides more than four of the tagged nucleic acid fragments and each tag is unique for a nucleic acid fragment.

92. (New) The method according to claim 68 wherein one or more of the steps is automated.

93. (New) The method according to claim 68 wherein the tagged fragments are generated from oligonucleotide primers that are conjugated to a tag at other than the 3' end of the primer.

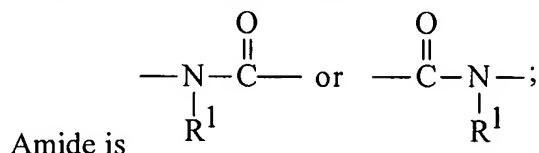
94. (New) The method according to claim 68 wherein the tagged fragments are generated from tagged dideoxynucleotide terminators.

95. (New) The method according to claim 68 wherein the tagged fragment has the formula:



wherein T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_{\alpha}F_{\beta}I_{\delta}$ such that the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms;

G is $(CH_2)_{1-6}$ wherein one and only one hydrogen on the CH_2 groups represented by each G is replaced with $-(CH_2)_c$ -Amide- T^4 ;



R^1 is hydrogen or C_{1-10} alkyl;

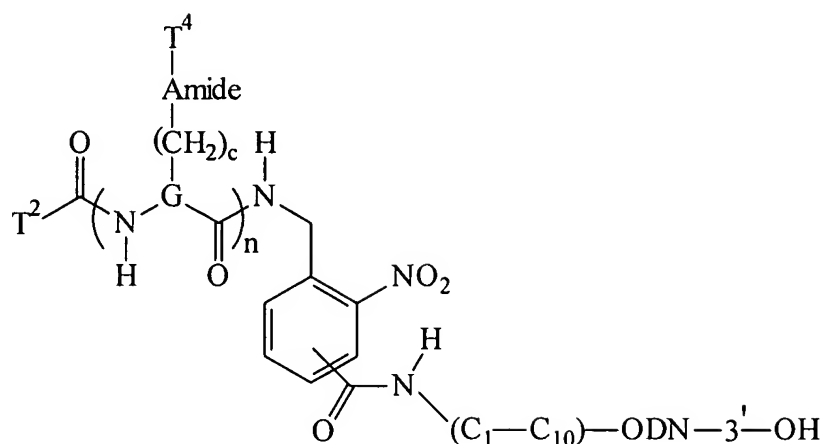
c is an integer ranging from 0 to 4;

C_1 - C_{10} is a hydrocarbylene group having from 1 to 10 carbon atoms;

ODN-3'-OH is a nucleic acid fragment having a terminal 3' hydroxyl group; and

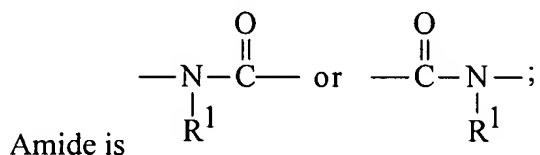
n is an integer ranging from 1 to 50 such that when n is greater than 1, then G, c, Amide, R^1 and T^4 are independently selected.

96. (New) The method according to claim 68 wherein the tagged fragment has the formula:



wherein T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_{\alpha}F_{\beta}I_{\delta}$ such that the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms;

G is (CH₂)₁₋₆ wherein one and only one hydrogen on the CH₂ groups represented by each G is replaced with -(CH₂)_c-Amide-T⁴;



Amide is

R¹ is hydrogen or C₁₋₁₀ alkyl;

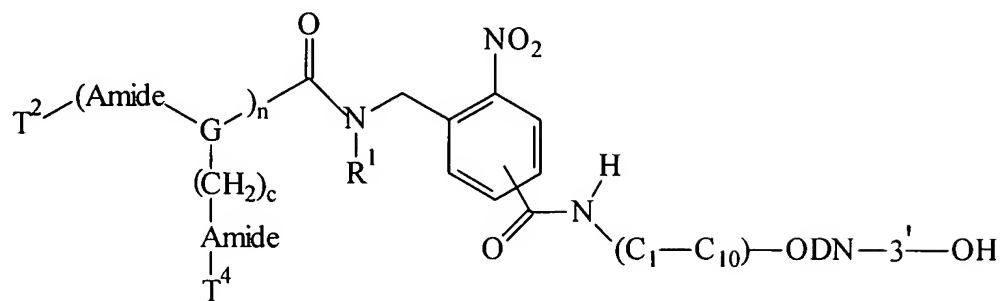
c is an integer ranging from 0 to 4;

C₁-C₁₀ is a hydrocarbylene group having from 1 to 10 carbon atoms;

ODN-3'-OH is a nucleic acid fragment having a terminal 3' hydroxyl group; and

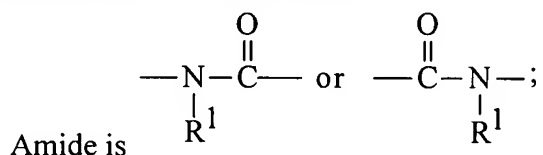
n is an integer ranging from 1 to 50 such that when n is greater than 1, then G, c, Amide, R¹ and T⁴ are independently selected.

97. (New) The method according to claim 68 wherein the tagged fragment has the formula:



wherein T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_{\alpha}F_{\beta}I_{\delta}$ such that the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms;

G is $(CH_2)_{1-6}$ wherein one and only one hydrogen on the CH_2 groups represented by each G is replaced with $-(CH_2)_c$ -Amide- T^4 ;



R^1 is hydrogen or C_{1-10} alkyl;

c is an integer ranging from 0 to 4;

C_1 - C_{10} is a hydrocarbylene group having from 1 to 10 carbon atoms;

ODN-3'-OH is a nucleic acid fragment having a terminal 3' hydroxyl group; and

n is an integer ranging from 1 to 50 such that when n is greater than 1, then G, c, Amide, R^1 and T^4 are independently selected.